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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/035,098 | 12/28/2001 | Geoffrey P. Symonds | J&J 2084 | 1700 |

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| EXAMINER | |
|---|---|
| SCHNIZER, RICHARD A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | |

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|---|---|
| 05/15/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/035,098 | SYMONDS ET AL. | |
| | Examiner | Art Unit | |
| | Richard Schnizer, Ph. D. | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-6,21,22,24-30,32-40,58,60,63-66 and 68-88* is/are pending in the application.

4a) Of the above claim(s) *4-6,33-40,58,60,64-66,68 and 79-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,21,22,24-30,32,64-66 and 69-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/8/02;5/22/039/9/05;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

An amendment was received and entered on 3/5/07. Applicant's election with traverse of group 1, "Tat protein", and the species "retroviral vector" is acknowledged. Applicant's grounds of traversal set forth in the responses of 2/14/05 and 5/31/06 were completely addressed in the subsequent restriction requirements of 1/5/06, and 9/6/06, respectively. Traversal o fhte latest restrcition requirement of 9/6/06 is on the grounds that "Applicants do not believe that searches for the pending claims would create a susbtantial burden for the Examiner." This is unpersuasive because it is not supported by any reasoning or logic, and does nto specifically address the grounds for restrcition that were laid out in detail in the restriction requirements of 1/5/06 and 9/6/06. The restriction is still deemed proper and is therefore made FINAL.

Claims 1-6, 21, 22, 24-30, 32-40, 58, 60, 63-66, and 68-88 are pending in the ppplication.

Claims 1-3, 21, 22, 24-30, 32, 64-66, and 69-78 read on the elected invention.

Claims 4-6, 33-40, 58, 60, 64-66, 68, and 79-88 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on 2/14/05, 5/31/06, and 3/5/07.

Note that claim 88 is not considered to be part of the elected invention because it is drawn to an invention that is independent and distinct from the elected invention. Claim 88 requires a double stranded RNA complex and a Tat protein classifiable in class 530, subclass 350. In contrast the elected invention does not require a Tat

protein, but instead requires a double stranded RNA encoding a Tat protein. These compositions are distinct in strcuutre and function andare not disclsoed as capable of use together, and so are properly restricted.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Australia on 2/9/2001. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

### *Compliance with Sequence Rules*

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **The specification at page 20, lines 3-9, discloses amino acid sequences in excess of 3 amino acids that not accompanied by a SEQ ID NO.** If these sequences are listed in the current Sequence Listing, then the specification should be amended to include the appropriate SEQ ID NO in each of the passages referred to above. If these sequences are not in the current Sequence Listing, then Applicant must provide:

A substitute computer readable form (CRF) copy of the "Sequence Listing".

A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 21, 22, 24-30, 32, 64-66, and 69-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-3, 21, 22, 24-30, 32, 64-66, and 69-78 are drawn to a double stranded RNA complex comprising (a) a first portion which is capable of hybridizing under physiological conditions to at least a portion of an mRNA, (b) a second portion which is capable of hybridizing to the first, wherein said two portions are located on separate molecules, and (c) an additional ribonucleic acid sequence that enhances the ability of dsRNA to alter the expression of the gene encoding the mRNA molecule, wherein the additional ribonucleic acid sequence encodes HIV Tat protein.

The claims do not specify whether the nature of the recited alteration of expression of the recited gene is positive or negative. The specification as a whole and the prior art of record (e.g. Bosher et al (2000), Caplen et al (2000), Fire (1998)) taught the use of double stranded RNA to inhibit gene expression of target genes. There is no evidence or suggestion of record that a dsRNA can be used to augment the expression of any gene to which it has homology, thus one of skill in the art would not believe that the scope of the invention that embraces a positive alteration of gene expression is operable. The specification provides no working example of this embodiment. Accordingly one could not make that embodiment of the invention without undue experimentation.

The art taught that mammalian cells could defend themselves against invasion by dsRNA through several mechanisms including double stranded RNA-activated protein kinase (PKR)-dependent and PKR-independent mechanisms. See Sledz et al

(Biochem. Soc. Trans. 32(6): 952-956, 2004, at e.g. Fig. 2 on page 955). For example, when activated by the presence of double stranded RNA, PKR phosphorylates and inactivates elongation initiation factor 2, thereby inhibiting cellular translation. This would be considered to have a global negative effect on gene expression in the affected cell. Other effects include induction of an interferon response subsequent and apoptosis. In other words, dsRNA can inhibit protein expression specifically by an RNAi mechanism, or globally through PKR-dependent and -independent mechanisms. Because Tat is known to inhibit this activity of PKR, it is unclear why one of skill in the art would expect Tat to enhance the ability of a dsRNA to negatively affect expression of a target gene. If the claimed method allowed expression of sufficient Tat to have nay effect, one of skill would reasonably expect the effect to be a relief of the translational block. Thus, any target RNAs that had not yet been degraded by the RNAi mechanism would have a greater likelihood of being translated. This in no way correlates with an enhancement of any ability of an dsRNA to alter the expression of a gene encoding a target mRNA. Thus one of skill in the art would not believe that the scope of the invention that embraces a negative alteration of gene expression is operable. The specification provides no working example of this embodiment. Accordingly one could not make that embodiment of the invention without undue experimentation.

In the event that the Examiner has overlooked an enabled embodiment, the following issues remain.

In view of the specification as filed, in order to function as claimed, the Tat protein encoded by the dsRNA must be expressed. However, the claimed dsRNAs do

not provide adequate structure to ensure expression of encoded Tat. One of skill in the art appreciates that the RNA encoding Tat would have to be translated to provide Tat protein, and so the RNA encoding Tat would need an operably linked ribosome binding site such as a 5' cap or an internal ribosome entry site, as well as possibly a polyadenylation signal and other translation-/mRNA stability-influencing sequences.

One of skill in the art would not expect a double stranded RNA to be a good substrate for translation because the number of hydrogen bonds formed in the duplex is far larger than the three hydrogen bonds formed between a translation template and a tRNA. Therefore maintenance of dsRNA structure would be thermodynamically more favorable than would be translation of the RNA. Accordingly, one would not expect to achieve efficient expression of Tat, such that it would be unpredictable as to whether or not it could exert its function to the degree required for the invention to function as claimed.

Finally, neither the prior art of record nor the specification provides guidance as to how to simultaneously use a dsRNA for both translation of an encoded sequence, and inhibition of a homologous sequence. Presumably the dsRNA is a substrate for dicer, and/or RISC upon entry into a cell, and these complexes would compete with ribosomes and translation initiation factors for the dsRNA. The specification provides no guidance as to how to make the dsRNA such that both translation and dsRNA inhibition can both occur. The instant claims do not limit the strand on which the sequence encoding the Tat protein is located, they set forth no limitation regarding any sequences necessary to ensure translation of the Tat sequence, nor any limitation regarding the

relative positions of the Tat sequence and the hybridizing sequences, or the lengths of the strands of the dsRNA. One of skill in the art is left to optimize these variables to obtain simultaneous Tat expression and dsRNA inhibition in the absence of guidance in the prior art or the specification. Accordingly, one of skill would have to perform undue experimentation in order to make the claimed invention.

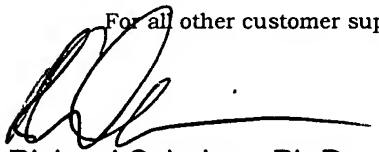
### *Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.





Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635